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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ABRAHAM, SALIEU M	

ART UNIT	PAPER NUMBER
3768	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,699	VAN ZIJL ET AL.	
	Examiner	Art Unit	
	Salieu M. Abraham	3768	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/22/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1– 8, 10 – 12, 22 - 27 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Song, H. K. et al.; Multislice Double Inversion Pulse Sequence for Efficient Black-Blood MRI. MRM 47, 616-620; 2002 **(Song).**

In Reference to Claim 1

Song teaches:

A magnetic resonance method including:

a) performing a blood-nulling magnetic resonance excitation sequence (70) that substantially nulls a magnetic resonance signal from blood; (see figure 1 and page 616)

and

b) subsequent to the performing of the blood-nulling magnetic resonance excitation sequence (70), performing a readout magnetic resonance sequence (72) to acquire a

magnetic resonance signal from tissue other than the nulled blood. (see figure 1)

In Reference to Claim 2

Song teaches:

The magnetic resonance method as set forth in claim 1, wherein the performing of a blood-nulling magnetic resonance sequence (70) includes:

a) performing an inversion recovery magnetic resonance excitation sequence (70) having an inversion time (60) to substantially null the magnetic resonance signal from blood. (see pages 616-617 and figure 1)

In Reference to Claim 3

Song teaches:

The magnetic resonance method as set forth in claim 2, wherein the performing of an inversion recovery magnetic resonance sequence (70) includes:

a) applying an inversion radio frequency pulse (74); delaying for the inversion time (60); and applying an excitation radio frequency pulse (80). (see page 616, paragraph 2)

In Reference to Claim 4

Song teaches:

The magnetic resonance method as set forth in claim 3, wherein:

a) the applying of the inversion radio frequency pulse (74) is performed without an accompanying spatially selective magnetic gradient pulse; (see page 616 and figure 1)

and

b) the applying of the excitation radio frequency pulse (80) is performed with an accompanying spatially selective magnetic field gradient pulse (82). (see pages 616-617 and figure 1)

In Reference to Claim 5

Song teaches:

The magnetic resonance method as set forth in claim 3, wherein the performing of an inversion recovery magnetic resonance sequence (70) further includes:
a) applying additional inversion radio frequency pulses to maintain blood in a substantially nulled condition. (see page 616, paragraph 2 and figure 1)

In Reference to Claim 6

Song teaches:

The magnetic resonance method as set forth in claim 3, wherein the inversion radio frequency pulse (74) is a 180 degree pulse and the excitation radio frequency pulse (80) is a 90 degree pulse. (see page 616, paragraph 2)

In Reference to Claim 7

Song teaches:

The magnetic resonance method as set forth in claim 2, further including determining the inversion time (60) for nulling blood by:

a) determining a T1 value of blood; and selecting the inversion time (60) for substantial blood nulling based on the determined T1 value of blood. (see page 617 and figure 2)

In Reference to Claim 8

Song teaches:

The magnetic resonance method as set forth in claim 7, wherein the determining of a T1 value of blood includes: acquiring a representative blood sample; and measuring the T1 value of the representative blood sample. (see page 617 and figure 2)

In Reference to Claim 9 (Song in view of Van Zilj)

Fritz'762 teaches:

A method provided for displaying vessel wall thickness from ultrasound imaging data, comprising:

a) generating LI and MA boundaries for the vessel wall using such ultrasound imaging data; (see claim 1)

b) measuring from the generated LI and MA boundaries an IMT along the vessel wall; (see section 0003and claims 1 and 20)

and

. (see sections 0019 and 0069- 0070 and claims 10,18 and 29).

In Reference to Claim 10

Song teaches:

The magnetic resonance method as set forth in claim 2, further including:

a) identifying at least a main magnetic field strength and a repeat time; (see pages 616 – 617) and

b) determining the inversion time (60) for nulling blood based on a predetermined relationship (64) between the inversion time for nulling the blood and the identified main magnetic field strength and repeat time.. (see page 617 and figure)

In Reference to Claim 11

Song teaches:

The magnetic resonance method as set forth in claim 2, further including:

a) optimizing an inversion time of a calibration inversion recovery magnetic resonance excitation sequence to minimize a magnetic resonance signal of a large blood vessel;

(see page 617 and figures 2 and 4-6)

and

b) selecting (66) the inversion time (60) for nulling blood as the optimized inversion time of the calibration inversion recovery magnetic resonance excitation sequence. (see page 617 and figure 2)

In Reference to Claim 12

Song teaches:

The magnetic resonance method as set forth in claim 2, further including: generating a reconstructed image from the acquired magnetic resonance signal. (see figures 4-6)

In Reference to Claim 22

Song teaches:

The magnetic resonance method as set forth in claim 2, wherein performing the readout magnetic resonance sequence (72) includes performing one or more of:

a) a single-shot imaging sequence, a single-shot echo planar sequence, a multi-shot imaging sequence, a spectroscopy sequence, a multiple slice image, a one-dimensional, two-dimensional, or three dimensional spatial encoding sequence, a fractional k-space acquisition sequence, a spin echo readout sequence, and a gradient echo readout sequence. (see page 616)

In Reference to Claim 23

Song teaches:

A magnetic resonance system including:

a) a blood nulling means (10, 12, 16, 18, 30, 32, 34) for performing a blood nulling magnetic resonance excitation sequence (70) that substantially nulls a magnetic resonance signal from blood; (see abstract and page 616)

and

b) a readout means (10, 12, 16, 18, 30, 32, 36) for performing a readout magnetic resonance sequence (72) to acquire a magnetic resonance signal from tissue other than the nulled blood, the readout means (10, 12, 16, 18, 30, 32, 36) operating subsequent to operation of the blood nulling means (10, 12, 16, 18, 30, 32, 34). (see abstract, figure 1 and page 617, paragraph 2)

In Reference to Claim 24

Song teaches:

The magnetic resonance system as set forth in claim 23, wherein the blood nulling means (10, 12, 16, 18, 30, 32, 34) includes:

a) an inversion recovery means (10, 12, 16, 18, 30, 32, 34) for performing an inversion recovery magnetic resonance excitation sequence (70) having an inversion time (60) in which magnetic resonance of blood is substantially nulled. (see page 617 and figure 2)

In Reference to Claims 25 – 27

Song teaches:

The magnetic resonance system as set forth in claim 24, further including:

(**Re Claim 25**) a means (64) for determining the inversion time (60) based on a set of values including at least a magnetic field strength value and a repeat time value. (see figure 2 and page 617)

(**Re Claim 26**) - a means (62) for measuring a T1 value of blood, the inversion time (60) being obtained from the measured T1 value of blood. (see pages 617 and Discussion section on page 619)

(**Re Claim 27**) - further including: a reconstruction means (44) for generating a reconstructed image from the acquired magnetic resonance signal. (see pages 617-619, and figures 3-6)

In Reference to Claim 31

Song teaches:

The magnetic resonance system as set forth in claim 27, further including: a means (154) for combining the reconstructed image with a reference image (152) to identify an abnormality in the reconstructed image. (see pages 617-618 and figures 3-6)

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 9, 13 - 21, and 28 - 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song, H. K. et al.; Multislice Double Inversion Pulse Sequence for Efficient Black-Blood MRI. MRM 47, 616-620; 2002 **(Song)** in view of Van Zijl, P.C.M., et al., "Quantitative Assessment of Blood Flow, Blood Volume and Blood Oxygenation Effects in Functional Magnetic Resonance Imaging", Nature Medicine 4(2), 159-167 (1998) **(Van Zilj)**

In Reference to Claim 9

Song has been shown to teach all of the limitations of claim 7. However, Song fails to teach:

The magnetic resonance method as set forth in claim 7, wherein the determining of a T1 value of blood further includes: determining a hematocrit of the blood; and correcting the T1 value of blood for the determined hematocrit..

Van Zilj, in the same field of endeavor, discloses a method for quantitative blood flow and volume assessment (see abstract). Van Zilj asserts one of his study's chief benefits is in using BOLD-MRI in tissue perfusion studies and furthering the state of the art through relating measured MRI effects to physiological parameters such as cerebral

blood volume, blood flow, hematocrit, etc., etc. He further cites a major advantage of his study's providing a means to obtain "high resolution absolute blood volume images" of the mammalian brain by "using hemoglobin (and hematocrit by extension) as a natural intravascular contrast agent." (see abstract and page 159)

Therefore, it would be obvious to one of ordinary skill in the art to include the hematocrit determination of Van Zilj in the method of Song in order to enhance the resulting image resolution for the vasculature under study as taught by Van Zilj.

In Reference to Claim 13

Song has been shown to teach all of the limitations of claim 2. Song also has been shown to establish a proper sequence basis for blood signal nulling using inversion recovery followed by rf excitation pulse sequences. However, Song fails to explicitly disclose introducing a physical perturbation and correlating the perturbation with a physiological response in reconstructed images.

Van Zilj, discloses using hypoxic hypoxia as a physiological perturbation factor for directly correlating blood physiological parameters such as blood volume with changes produced by the perturbation (see abstract and page 159). He cites hypoxic significant impact on the resulting MRI signal as a key plus in producing images from which the effects of perturbation and blood physiological parameters can be clearly associated in order to facilitate obtaining higher resolution images in smaller vessels in vivo as well.

Therefore, it would be obvious to one of ordinary skill in the art to include a physiological perturbation subsequent to applying an IR recovery pulse sequence of Van Zilj in the method of Song in order to expand the ability to produce higher (resolution) quality images to smaller vessels in the vasculature that require study as taught by Van Zilj.

In Reference to Claims 14 -15

Song in view of Van Zilj has been shown to teach all of the limitations of claim 12. Song in view of Van Zilj further teaches :

The magnetic resonance method as set forth in claim 12:

(**Re Claim 14**) - further including: subsequent to performing the readout magnetic resonance sequence (72), inducing a physiological perturbation; subsequent to inducing the physiological perturbation, repeating performing the inversion recovery magnetic resonance excitation sequence (70); subsequent to repeating the performing of the inversion recovery magnetic resonance excitation sequence (70), performing a plurality of readout magnetic resonance sequences (72) each having a different echo time to acquire a plurality of magnetic resonance signals corresponding to the plurality of echo times; generating a plurality of perturbation reconstructed images from the acquired plurality of magnetic resonance signals corresponding to the plurality of echo times; and determining a temporal evolution of a physiological response to the physiological perturbation based on the plurality of perturbation reconstructed images. (see Song figure 1 and figures 3-5)

(**Re Claim 15**) - wherein the determining of a temporal evolution includes: computing a change in vascular space occupancy signal between perturbation reconstructed images and corresponding unperturbed reconstructed images for each echo time to produce change in vascular space occupancy signal versus echo time data (106); and fitting the change in vascular space occupancy signal versus echo time data (106) to a mathematical model to obtain a blood volume parameter value (118). (see Van Zilj figures 1 and 2)

Therefore, Song in view of Van Zilj meets all claim 14-15 limitations.

In Reference to Claims 16 - 17

Song has been shown to teach all of the limitations of claim 2. Van Zilj further teaches :

(**Re Claim 16**) - The magnetic resonance method as set forth in claim 12, further including: determining a T1 value of tissue (132, 134); computing a tissue magnetization (M) based on the T1 value of the tissue (132, 134); generating a normalized reconstructed image (142) by dividing the reconstructed image by the tissue magnetization; and estimating a blood volume parameter value (146) based on the normalized reconstructed image (142). (see pages 160 – 162, equation 12, and page 163, first paragraph)

(**Re Claim 17**) - The magnetic resonance method as set forth in claim 16, wherein the reconstructed image corresponds to a subject brain region, and determining the T1 value of the tissue (132, 134) includes: determining a first T1 value (132) corresponding to white brain matter; and determining a second T1 value (134) corresponding to gray brain matter; wherein the dividing of the reconstructed image by the tissue magnetization uses for each image element a selected one of the first and second T1 values (132, 134) based on a classification of local tissue type as one of gray brain matter and white brain matter. (see figure 3 and Table 1)
Therefore, Song in view of Van Zilj meets all claim 16-17 limitations.

In Reference to Claims 18 - 20

Song has been shown to teach all of the limitations of claim 2. Song in view of Van Zilj further teaches:

(**Re Claim 18**) – The magnetic resonance method as set forth in claim 12, wherein performing the readout magnetic resonance sequence (72) effects imaging of a subject

brain region of a subject brain, and the method further includes: providing a reference image (152) of a reference brain region; and comparing the reconstructed image with the reference image (152) to detect an abnormality of the subject brain region. (see Van Zilj pages 163-164 and Tables 1 and 2)

(**Re Claim 19**) – The magnetic resonance method as set forth in claim 18, wherein providing the reference image (152) of a reference brain region includes repeating: performing the inversion recovery magnetic resonance excitation sequence (70), performing the readout magnetic resonance sequence (72), and generating the reconstructed image on the reference brain region to generate the reference image (152). (see Song pages 617-618 and figures 3-6)

(**Re Claim 20**) - The magnetic resonance method as set forth in claim 19, wherein the reference brain region is selected from a group consisting of: a brain region of a contralateral side of the subject brain corresponding to the subject brain region, a brain region of a brain other than the subject brain which corresponds to the subject brain region, and a brain region of the subject brain other than the subject brain region. (see Van Zilj Table 2 and figures 3 and 4)

Therefore, Song in view of Van Zilj meets all claim 18-20 limitations.

In Reference to Claim 21

Song has been shown to teach all of the limitations of claim 2. Song in view of Van Zilj further teaches:

The magnetic resonance method as set forth in claim 12, further including: computing at least one of a proton density weighting of tissue, a T1 weighting of tissue, and a T2

weighting of tissue without interference from a magnetic resonance signal of blood based on the reconstructed image. (see Van Zilj, page 163 last paragraph)

Therefore, Song in view of Van Zilj meets all claim 21 limitations.

In Reference to Claims 28 -30

Song has been shown to teach all of the limitations of claim 27. Song in view of Van Zilj further teaches:

(**Re Claim 28**) – The magnetic resonance system as set forth in claim 27, further including: a means (100, 130) for computing a blood volume parameter value (118, 146) from the reconstructed image. (see Van Zilj , page 163)

(**Re Claim 29**) – The magnetic resonance system as set forth in claim 28, wherein the means (130) for computing a blood volume parameter value (118, 146) includes: a means (136, 140) for normalizing the reconstructed image based on a T1 value of tissue (132, 134) to generate a tissue-normalized reconstructed image; and a means (144) for computing the blood volume from the tissue-normalized reconstructed image. (see Van Zilj , pages 163 –166)

(**Re Claim 30**) - The magnetic resonance system as set forth in claim 28, wherein the means (100) for computing a blood volume parameter value (118, 146) includes: a means (104) for computing an intermediate parameter (106) functionally related to blood volume for a plurality of reconstructed images produced by repetitively invoking the readout means and the reconstruction means with a corresponding plurality of echo times (102); and a means (110) for fitting a parameterized model to the intermediate

parameters (106) and the corresponding echo times (102), the parameterized model having parameters including a rest blood volume (118) and a blood volume change (124). (see Van Zilj , tables 1 and 2 and pages 163 – 166).

Therefore, Song in view of Van Zilj meets all claim 28 -30 limitations.

Conclusion

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Foo et al., Ito et al., Ookawa et al., Saranathan et al. and Ventkataraman et al. have been included because they all teach the use of diagnostic magnetic resonance imaging-based methods and systems which make use of region isolation and/or suppression protocols for vascular studies similar in scope to applicant's proposed invention.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Salieu M. Abraham whose telephone number is (571) 270-1990. The examiner can normally be reached on Monday through Thursday 9:30 am - 7:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on (571) 272-4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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